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Brief Communication

Lagged Association Between Geomagnetic Activity and Diminished Nocturnal Pain Thresholds in Mice

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A wide variety of behaviors in several species has been statistically associated with the natural variations in geomagnetism. To examine whether changes in geomagnetic activity are associated with pain thresholds, adult mice were exposed to a hotplate paradigm once weekly for 52 weeks during the dark cycle. Planetary A index values from the previous 6 days of a given hotplate session were correlated with the mean response latency for subjects to the thermal stimulus. We found that hotplate latency was significantly ($P < 0.05$) and inversely correlated ($rho = -0.25$) with the daily geomagnetic intensity 3 days prior to testing. Therefore, if the geomagnetic activity was greater 3 days before a given hotplate trial, subjects tended to exhibit shorter response latencies, suggesting lower pain thresholds or less analgesia. These results are supported by related experimental findings and suggest that natural variations in geomagnetic intensity may influence nociceptive behaviors in mice. Bioelectromagnetics 28:577–579, 2007. © 2007 Wiley-Liss, Inc.

Key words: geomagnetism; nociception; correlation

Changes in geomagnetic intensity have been correlated with an array of physiological and behavioral responses in several species including humans [Barnothy, 1974]. Since all living matter is surrounded by the earth's magnetic field, it is not surprising that a considerable breadth of information regarding the consequences of geomagnetic activity on biological systems has been reported. Our laboratory has found significant associations between natural and artificially induced geomagnetic-like patterns and various behaviors from seizure susceptibility and mortality in rats [Bureau and Persinger, 1992, 1995; Persinger, 1996] to altered sensory and affective states in humans [Persinger and Richards, 1995; Persinger, 2004]. Of particular interest was the question of whether an association exists between alterations in geomagnetism and pain thresholds. Although prior work had demonstrated that exposing rodents to various exogenous magnetic field patterns could significantly diminish [Choi et al., 2003] or enhance [Martin et al., 2004] the analgesic response of their subjects, the consequences of naturally varying geomagnetic activity on basal pain thresholds has received limited attention [Ossenkopp et al., 1983].

To address this question we utilized a hotplate paradigm to assess pain thresholds in normal mice. A total of 16 adult male and female CD-1 mice, approximately 4 months of age and weighing about 25 g, were used in the present experiment. They were housed in groups of four according to sex under standard laboratory conditions, L:D/12:12, with light onset at 07:30 h local time. To determine pain (nociceptive) thresholds, mice were placed on a hotplate (Omnitech analgesiometer) set at 55 °C once weekly for 52 weeks (April 2004–March 2005) during the middle of the dark cycle (00:00 h, Monday local time). The time required for a given subject to display the criterion response, characterized by the licking of one hind paw (but not forepaw), or to exhibit a

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leap or jump, was recorded to the nearest 0.01 s and taken as the hotplate latency. At this time animals were quickly removed from the device and returned to the home cage. For ethical considerations, any animal that failed to demonstrate the criterion response for removal from the apparatus within 60 s subsequently received this value and the trial was terminated. All procedures were conducted under low intensity red light conditions to avoid disruption of the nocturnal physiology of the subjects. These procedures were approved by the local animal care committee and were in compliance with the Canadian Council on Animal Care guidelines.

The planetary A index was used as a measure of daily geomagnetic activity. It approximates an average of the eight 3-h K indices which reflect the degree of geomagnetic disturbance beginning at 00:00 h UTC. We obtained the average planetary A index values (in nT) from Geomagnetic Indices Bulletin (Boulder, CO) for the 6 days before each testing session, which were then correlated (using Spearman *rho*) with the mean hotplate latency for all subjects for a given trial. We have previously calculated that sample measurements of the local geomagnetic conditions were highly correlated ($rho > 0.90$; $P < 0.001$) with those obtained from the Boulder site [Galic and Persinger, 2004].

We found that the strongest and only statistically significant correlation ($rho = -0.25$; $P < 0.05$) was observed between the geomagnetic activity 3 days before a given testing session and the mean hotplate latency for all subjects (Fig. 1). The correlation coefficients from 1 to 6 days before each session were 0.21, −0.08, −0.25, −0.17, −0.03, and −0.14, respectively. Because each testing session took place at approximately 00:00 h Monday local time, the functional relationship with this 3 day lag in geomagnetic effect was actually the mean geomagnetic strength of the preceding Friday. In other words, the mean geomagnetic activity of each Friday was negatively correlated ($rho = -0.25$; $P < 0.05$) with the average hotplate latency on Sunday at midnight/early Monday throughout the 12 month observation period. The monthly mean hotplate latencies (in seconds) and the planetary A indices (in nT) for each of the 12 months tested are presented in Figure 2. We also noted that approximately half ($n = 9$) of the 16 subjects died over the duration of the study as a result of what we assumed to be age- or stress-related factors. This occurred at a rate of approximately one subject per month beginning at about month 3.

In the present study using the hotplate paradigm as a behavioral assay for pain thresholds in mice, we observed a weak negative correlation ($rho = -0.25$; $P < 0.05$) between hotplate latency and the geomagnetic activity 3 days earlier. The pattern of our observations is consistent with earlier results from Ossenkopp et al. [1983] who reported a significant reduction in nocturnal pain thresholds in mice following a single geomagnetic disturbance. Moreover, in an experimental design, Prato et al. [2005] demonstrated that by shielding subjects using a Mu-metal enclosure designed to significantly attenuate both electric and magnetic fields (including the geomagnetic field), that shielded mice displayed a substantial analgesic response when compared to sham controls.

One interesting finding from the previous study which may support our observations of a lagged relationship between geomagnetic activity and hotplate latency is that shielded subjects required at least 2 days exposure to the ''hypogeomagnetic'' condition before a significant analgesic effect emerged [Prato et al., 2005]. Hysteretic or lag effects of geomagnetic fields on clinical and experimental phenomena are frequently reported in the literature [Barnothy, 1974; Kay, 1994; Galic and Persinger, 2004]. This suggests that the

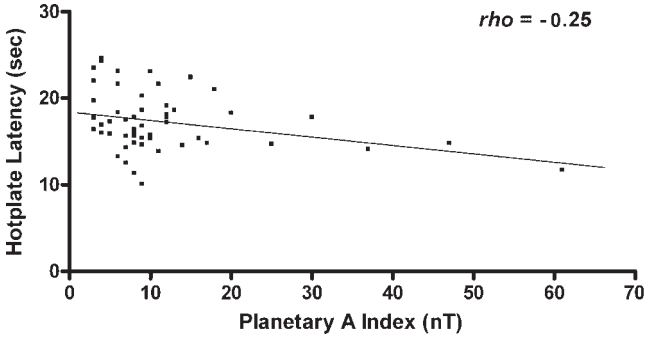

Fig. 1. A scattergram of the mean weekly hotplate latencies (in seconds) as a function of planetary A index (in nT) 3 days before testing over 52 trials. Hotplate latency was significantly ($P < 0.05$) and inversely correlated ($rho = -0.25$) with geomagnetic activity.

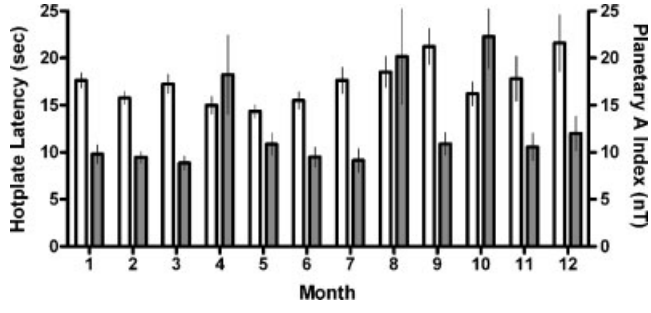

Fig. 2. Means and SEM for the monthly hotplate latencies of mice in seconds (light columns/left axis) and the monthly planetary A indices in nanotesla (dark columns/right axis) over a 12-month period (April 2004 – March 2005). Each month represents the average hotplate latencies for each trial conducted on every Monday at 00:00 h local time, as well as the average planetary A index value for a given month.

mechanism responsible for the effect of geomagnetic activity on nociception is not acute and may require time to generate changes in pain signaling pathways that influence behavior.

The central mechanisms by which changes in geomagnetic activity produce alterations in physiology and behavior are currently unknown. Proposed mechanisms implicate an interaction between geomagnetic disturbances and melatonin regulation in the brain. The pineal gland represents the largest source of melatonin in the central nervous system and may also function as a receptor for detecting geomagnetism [Olcese et al., 1988]. In humans, there is evidence that geomagnetic perturbations are associated with a decrease in melatonin release from the pineal gland [Burch et al., 1999]. Since it is known that melatonin has analgesic effects when administered to mice [Golombek et al., 1991], the possibility exists that the occurrence of a geomagnetic ''storm'' may cause a decrease in melatonin synthesis and thereby evoke a reduction in pain threshold.

Similar explanations have been used in the context of other medical disorders to which environmental magnetic effects have been linked including, sudden infant death syndrome [O'Connor and Persinger, 1997], suicide [Berk et al., 2006], sudden unexpected death in epilepsy patients [Persinger and Psych, 1995], and myocardial infarctions [Rapoport et al., 2006]. Subsequent studies are encouraged to design experiments that resolve the intricacies of the *bio-magnetic* interaction so that adverse effects from geomagnetic disturbances can be predicted and perhaps ameliorated.

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